



9200/1643

PATENT  
600-1-266N

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT : Kreek, M.J. *et al.*

SERIAL NO. : 09/883,839 EXAMINER : Unknown

FILED : June 18, 2001 ART UNIT : 1643

FOR : ALLELES OF THE HUMAN MU OPIOID RECEPTOR, DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS OF TREATMENT BASED THEREON

CERTIFICATE OF MAILING UNDER 37 CFR 1.8

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Betty Schultz  
(Name of Depositor)

Betty Schultz 4/5/04  
(Signature and Date)

REQUEST FOR WITHDRAWAL OF INCORRECT ABANDONMENT

MAIL STOP AF  
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Dear Sir:

Applicants request herewith that the Notice of Abandonment dated November 18, 2003 be vacated, as a proper response to the Notice to File Missing Parts dated July 20, 2001 was filed.

In the present instance, a Request for a One-Month Time Extension was submitted together with a Preliminary Amendment, an executed Declaration and Power of Attorney, a transmittal sheet, a PTOSB17 form, and a check in the amount of \$1,317.00. All items were effectively mailed on October 15, 2001. In support of Applicant's entitlement for withdrawal of the Notice of Abandonment, Applicant submits herewith copies of the One-Month Time Extension, the executed Declaration and Power of Attorney, the Preliminary Amendment, the transmittal sheet, the PTOSB17 form, and the corresponding canceled postcard receipts with respect to each.

Furthermore, Applicants' Representative respectfully notes that the second page of the

PATENT  
600-1-266N

Notice to File Missing Parts was not included in the original notice as received by Applicant.  
Please forward the missing page such that Applicants can respond to any deficiencies that may be outstanding.

Favorable consideration and withdrawal of the Notice of Abandonment, and restoration of the present application to the pending roles for purposes of further processing, are believed to be in order, and are courteously solicited.

Respectfully submitted,

Veronica Mallon  
VERONICA MALLON, Ph.D.  
Agent for Applicant(s)  
Registration No. 52,491

KLAUBER & JACKSON  
411 Hackensack Avenue  
Hackensack, NJ 07601  
(201) 487-5800  
Enclosures

Date: April 5, 2004



Serial No. 09/883,839 File No. 600-1-266N By DAJ/MAY/aj  
Title ALLELES OF THE HUMAN MU OPOID RECEPTOR, ...

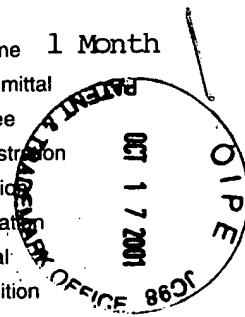
In the Matter of the Application of Mary Jeanne Kreek et al.

The following was received in the U.S. Patent & Trademark Office on the date stamped hereon: via first-class mail

Transmittal Sheet/Cover Ltr.  
 Application For Patent  
 Declaration  Affidavit  
 Drawings  Sheet(s)  
 S.E. Verified Statements  
 Assignment  
 Check for \$ 1,317.00  
 Letter  Missing Parts  
 Priority Document  
 Amendment  Response

Preliminary

Extension of Time 1 Month  
 Issue Fee Transmittal  
 Maintenance Fee  
 Appn. TM Registration  
 8 & 15 Declaration  
 Renewal Application  
 Notice of Appeal  
 Brief  Petition  
 Power of Attorney  
 PTOSB17



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CLAUBER & JACKSON

Serial No. 09/883,839 File No. 600-1-266N By DAJ/MAY/aj  
Title ALLELES OF THE HUMAN MU OPOID RECEPTOR, ...

In the Matter of the Application of Mary Jeanne Kreek et al.

The following was received in the U.S. Patent & Trademark Office on the date stamped hereon: via first-class mail

Executed

- Transmittal Sheet/Cover Ltr.  Extension of Time 1 Month  
 Application For Patent  Issue Fee Transmittal  
 Declaration  Affidavit  Maintenance Fee  
 Drawings  Sheet(s)  Appln. TM Registration  
 S.E. Verified Statements  8 & 15 Declaration  
 Assignment  Renewal Application  
 Check for \$ 1,317.00  Notice of Appeal  
 Letter  Missing Parts  Brief  Petition  
 Priority Document  Power of Attorney  
 Amendment  Response  PTOSB17

Preliminary

KLAUBER AND JACKSON  
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13135

55-216/212  
11

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DATE

10/15/01

THIS CHECK IS DELIVERED IN CONNECTION WITH THE FOLLOWING ACCOUNTS

600-1-266N			
09/883,839			
MAY			

1013135 10212021620 134000688 710

Joann Rodgers

mailed 10/15/01



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PTO/SB/21 (08-00)

Approved for use through 10/31/2002, OMB 0651-0031

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## TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

		Application Number	09/883,839
		Filing Date	June 18, 2001
		First Named Inventor	Mary Jeanne Kreek et al
		Group Art Unit	1643
		Examiner Name	TBA
Total Number of Pages in This Submission		Attorney Docket Number	600-1-266N

### ENCLOSURES (check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Assignment Papers (for an Application)	<input type="checkbox"/> After Allowance Communication to Group
<input checked="" type="checkbox"/> Fee Attached	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input checked="" type="checkbox"/> Amendment / Reply	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Status Letter
<input checked="" type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Terminal Disclaimer	Executed Declaration, Postcard & Check
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Certified Copy of Priority Document(s)	<input type="checkbox"/> CD, Number of CD(s) _____	
<input checked="" type="checkbox"/> Response to Missing Parts/ Incomplete Application	<input type="checkbox"/> Remarks	
<input checked="" type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

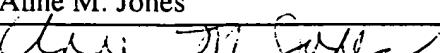
### SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	David A. Jackson, Reg. No. 26,742
Signature	
Date	10/15/2001

### CERTIFICATE OF MAILING

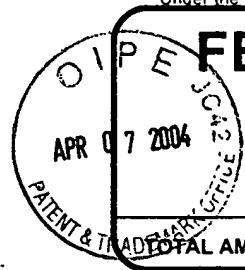
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date:

October 15, 2001

Typed or printed name	Anne M. Jones
Signature	
Date	October 15, 2001

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# FEET TRANSMITTAL for FY 2001

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT (\$1,317.00)

## Complete if Known

Application Number	09/883,839
Filing Date	June 18, 2001
First Named Inventor	Mary Jeanne Kreek et al.
Examiner Name	TBA
Group Art Unit	1643
Attorney Docket No.	600-1-266N

## METHOD OF PAYMENT

1.  The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number	11-1153
Deposit Account Name	

Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17

Applicant claims small entity status. See 37 CFR 1.27

2.  Payment Enclosed:

Check  Credit card  Money Order  Other

## FEE CALCULATION (continued)

## 3. ADDITIONAL FEES

Large Entity Fee Code (\$)	Small Entity Fee Code (\$)	Fee Description	Fee Paid
105	130	205 65 Surcharge - late filing fee or oath	65.00
127	50	227 25 Surcharge - late provisional filing fee or cover sheet	
139	130	139 130 Non-English specification	
147	2,520	147 2,520 For filing a request for <i>ex parte</i> reexamination	
112	920*	112 920* Requesting publication of SIR prior to Examiner action	
113	1,840*	113 1,840* Requesting publication of SIR after Examiner action	
115	110	215 55 Extension for reply within first month	55.00
116	390	216 195 Extension for reply within second month	
117	890	217 445 Extension for reply within third month	
118	1,390	218 695 Extension for reply within fourth month	
128	1,890	228 945 Extension for reply within fifth month	
119	310	219 155 Notice of Appeal	
120	310	220 155 Filing a brief in support of an appeal	
121	270	221 135 Request for oral hearing	
138	1,510	138 1,510 Petition to institute a public use proceeding	
140	110	240 55 Petition to revive - unavoidable	
141	1,240	241 620 Petition to revive - unintentional	
142	1,240	242 620 Utility issue fee (or reissue)	
143	440	243 220 Design issue fee	
144	600	244 300 Plant issue fee	
122	130	122 130 Petitions to the Commissioner	
123	50	123 50 Processing fee under 37 CFR 1.17(q)	
126	180	126 180 Submission of Information Disclosure Stmt	
581	40	581 40 Recording each patent assignment per property (times number of properties)	
146	710	246 355 Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249 355 For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279 355 Request for Continued Examination (RCE)	
169	900	169 900 Request for expedited examination of a design application	
Other fee (specify) _____			
*Reduced by Basic Filing Fee Paid			
SUBTOTAL (3) (\$120.00)			

\*or number previously paid, if greater; For Reissues, see above

SUBMITTED BY	Complete (if applicable)		
Name (Print/Type)	David A. Jackson	Registration No. (Attorney/Agent)	26,742 Telephone 201-487-5800
Signature		Date	October 15, 2001

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600-1-266 N

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: MARY JEANNE KREEK et al.

SERIAL NO.: 09/883,839 EXAMINER: Unknown

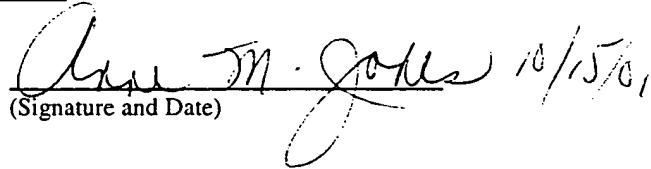
FILED: June 18, 2001 ART UNIT: 1643

FOR: ALLELES OF THE HUMAN MU OPIOID RECEPTOR, DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS OF TREATMENT BASED THEREON

Certificate of Mailing Under 37 CFR 1.8

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David A. Jackson, Reg. No. 26,742  
(Name of Registered Rep.)

  
(Signature and Date)

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, DC 20231

Dear Sir:

Prior to calculating claim fees, please enter the following amendments into the file of the present application.

IN THE CLAIMS:

Please cancel claims 1-83 without prejudice or disclaimer and add the following new claims 84-141.

84. A variant allele of a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.

85. The variant allele of claim 84 wherein said variant allele is isolated.
86. The isolated variant allele of Claim 85, detectably labeled.
87. An isolated nucleic acid molecule selectively hybridizable to the isolated variant allele of Claim 85.
88. The isolated nucleic acid molecule of Claim 87, detectably labeled.
89. A variant allele of a human mu opioid receptor gene which encodes a variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.
90. The variant allele of claim 89 wherein said variant allele is isolated.
91. A isolated variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.
92. An antibody having a variant human mu opioid receptor of Claim 91 as an immunogen.
93. The antibody of Claim 92, detectably labeled
94. A cloning or expression vector comprising an isolated variant allele of a human mu opioid

receptor gene and an origin of replication, wherein said variant allele comprises a DNA of claim 84.

95. A cloning or expression vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84.
96. An expression vector comprising an isolated variant allele of a human mu opioid receptor gene comprising a DNA sequence of claim 84.
97. An expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence of claim 84.
98. A unicellular host transformed or transfected with an expression vector comprising an isolated variant allele of a human mu opioid receptor gene operatively associated with a promoter, wherein said variant allele comprises a DNA sequence of claim 84.
99. A unicellular host transformed with an expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence of claim 84.

100. An isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein said variations comprise T67C; T124A; C153T; G174A or 187INS:GGC.
101. The isolated variant allele of Claim 100 detectably labeled.
102. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene comprising a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1.
103. The isolated nucleic acid molecule of Claim 102, detectably labeled.
104. An isolated variant allele of a human mu opioid receptor gene, which encodes a variant human mu opioid receptor comprising an amino acid sequence having at least two variations in SEQ ID NO:2, wherein at least one said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.
105. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene of claim 84, wherein and said variant allele comprises a DNA sequence having at least two variations in SEQ ID NO:1, and at least one of said variations comprises T67C; T124A; C153T; G174A or 187INS:GGC, so that said isolated nucleic acid molecule encodes a variant human mu opioid receptor comprising at least two variations in sequence of SEQ ID NO:2, wherein at least one of said variations comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.

106. A variant human mu opioid receptor of claim 91 comprising an amino acid sequence having at least two variations in SEQ ID NO:2, wherein at least one of said variations comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.
107. An antibody having a variant human mu opioid receptor of Claim 106 as an immunogen.
108. The antibody of Claim 107, detectably labeled.
109. A cloning or expression vector comprising an isolated variant allele of a human mu opioid receptor gene and an origin of replication, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein at least one of said variations comprises T67C; T124A; C153T; G174A; or 187INS:GGC.
110. A cloning or expression vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein at least one of said variations comprises T67C; T124A; C153T; G174A; or 187INS:GGC.
111. A unicellular host transformed with an expression vector of Claim 109.
112. A unicellular host transformed with an expression vector of Claim 110.
113. A method for determining a susceptibility in a subject to at least one addictive disease,

comprising the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;
- b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence of claim 84,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to at least one addictive disease relative to the susceptibility to said at least one addictive disease in a standard.

114. The method for determining a susceptibility to at least one addictive disease of Claim 113, further comprising the step of determining whether said human mu opioid receptor gene of said second allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said human mu opioid receptor gene of said second allele is expected to be indicative of the subject's susceptibility to said at least one addictive disease relative to the susceptibility to said at least one addictive disease in said standard.
115. The method of either of Claim 114 wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
116. A method for determining a susceptibility to at least one addictive disease in a subject relative to susceptibility in a standard, comprising the steps of:
  - a) removing a bodily sample from said subject, wherein said sample comprises a human mu

- opioid receptor;
- b) determining whether said human mu opioid receptor comprises an amino acid sequence of claim 91,

such that the presence of said at least one variation is expected to be indicative of the susceptibility to said at least one addictive disease in said subject relative to susceptibility to said at least one addictive disease in said standard, wherein the human mu opioid receptor of said standard comprises an amino acid sequence of SEQ ID NO:2.

117. The method of Claim 116, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
118. A method for determining a susceptibility to pain in a subject relative to a susceptibility of pain in a standard, wherein the method comprises the steps of:
- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;
- b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence of claim 84,
- such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.
119. The method of Claim 118 for determining a susceptibility to pain in a subject, further comprising

the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility of pain in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

120. A method for determining a therapeutically effective amount of pain reliever to administer to a subject in order to induce analgesia in said subject relative to a therapeutically effective amount of pain reliever to administer to a standard in order to induce analgesia in said standard, wherein the method comprises determining a susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein susceptibility to pain in said subject is expected to be indicative of said therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject relative to said therapeutically effective amount of pain reliever to administer to said standard to induce analgesia in said standard.
121. The method of Claim 120 for determining a therapeutically effective amount of pain reliever to administer to said subject, wherein determining susceptibility to pain in said subject comprises the steps of:
  - a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and
  - b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation

comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof, wherein the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to pain relative to said to susceptibility of pain in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, such that said therapeutically effective amount of pain reliever to administer to the subject in order to induce analgesia is related to said susceptibility to pain in said subject relative to susceptibility to pain in said standard.

122. The method of Claim 121, wherein determining susceptibility to pain in said subject relative to susceptibility to pain in said standard further comprises the step of determining whether said second allele of said bodily sample from said subject comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C, T124A or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, and the therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject is related to the presence of said at least one variation in said human mu opioid receptor gene of said second allele of said bodily sample from said subject.
  
123. A method for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from at least one addictive disease to treat the at least one addictive disease in said subject relative to a therapeutically effective amount of therapeutic agent to administer to

a standard suffering from the at least one addictive disease to treat the at least one addictive disease in said standard, wherein the method comprises the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and
- b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A or 187INS:GGC,

wherein the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the therapeutically effective amount of said therapeutic agent to administer to the subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

124. The method of Claim 123 for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from said at least one addictive disease to treat said at least one addictive disease, relative to said therapeutically effective amount of said therapeutic agent administered to said standard suffering from said at least one addictive disease to treat said at least one addictive disease in said standard, further comprising the step of determining whether said second allele of said bodily sample from said subject comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele related to said therapeutically effective amount of said therapeutic

agent administered to said subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

125. The method of either of Claims 123 or 124, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbiturate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
126. A commercial test kit for determining the presence of at least one variation in a human mu opioid receptor gene of an allele in a bodily sample taken from a subject, wherein the commercial test kit comprises:
  - a) PCR oligonucleotide primers suitable for detection of an allele comprising a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1 comprising T67C; T124A; C153T; G174A; or 187INS:GGC;
  - b) other reagents; and
  - c) directions for use of the kit.
127. A commercial test kit for detecting a variant human mu opioid receptor in a bodily sample taken from a subject, comprising
  - (a) predetermined amount of at least one detectably labeled immunochemically reactive component having affinity for a variant human mu opioid receptor; said variant being at least one of Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63;

(b) other reagents; and

(c) directions for use of the kit.

128. A commercial test kit for detecting a variant human mu opioid receptor in a bodily sample taken from a subject, wherein said kit comprises:

- (a) a labeled component which has been obtained by coupling the human mu opioid receptor of the bodily sample to a detectable label;
- (b) one or more additional immunochemical reagents of which at least one reagent is a ligand or an immobilized ligand, which ligand comprises:
  - (i) a ligand capable of binding with the labeled component (a);
  - (ii) a ligand capable of binding with a binding partner of the labeled component (a);
  - (iii) a ligand capable of binding with at least one of the component(s) to be determined; or
  - (iv) a ligand capable of binding with at least one of the binding partners of at least one of the component(s) to be determined;
- (c) directions for the performance of a protocol for the detection and/or determination of one or more components of an immunochemical reaction between the human mu opioid receptor and a specific binding partner thereto.

129. A method for diagnosing a disease or disorder related to a physiological function regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus pituitary gonadal axis (HPG), wherein the method comprises the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;

b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus pituitary gonadal axis (HPG), wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

130. The method of Claim 129, wherein said physiological function comprises sexual or reproductive function, gastrointestinal motility, immune response, or ability to withstand stress.
131. The method of Claim 130, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to said standard, or decreased ability to withstand stress relative to said standard.
132. The method of Claim 130 for diagnosing a disease or disorder related to a physiological function regulated by the HPA or HPG, further comprising the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

133. The method of Claim 132, wherein said physiological function comprises sexual or reproductive function, gastrointestinal motility, immune response, or ability to withstand stress.
134. The method of Claim 132, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to said standard, or decreased ability to withstand stress relative to said standard.
135. The method of Claim 132, wherein said disease or disorder comprises diarrhea.
136. A method for selecting an appropriate therapeutic agent and a therapeutically effective amount of said agent to administer to said subject to treating a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein the method comprises diagnosing said disease or disorder in said subject, wherein said disease or disorder is expected to be indicative of said appropriate therapeutic agent for treating said disease or disorder.
137. The method of Claim 136, wherein said physiological function comprises reproductive or sexual function, gastrointestinal motility, immune response, or ability to withstand stress.
138. The method of Claim 136, wherein diagnosing said disease or disorder in said subject comprises the steps of:
  - a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and
  - b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said

at least one variation comprises T67C; T124A; or 187INS:GGC,  
wherein the presence of said at least one variation in said human mu opioid receptor gene of said  
first allele is expected to be indicative of said disease or disorder related to a physiological  
function regulated by the HPA or HPG axes.

139. The method of Claim 138, wherein diagnosing a disease or disorder related to a physiological function regulated by the HPA or HPG further comprises the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.
140. The method of Claim 139, wherein said physiological function comprises reproductive or sexual function, gastrointestinal motility, immune response, or ability to withstand stress.
141. The method of Claim 139, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to immune response in said standard, or decreased ability to withstand stress relative to ability to withstand stress of said standard.

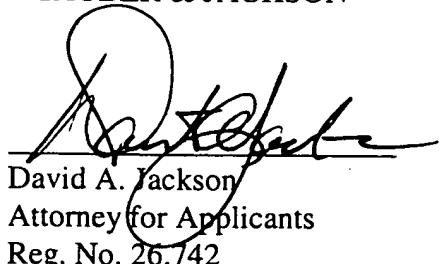
#### **Remarks**

The new claims presented above which replace the original claims contain no new matter

and were provided simply to reduce the number of claims in the application. Examination on the merits is courteously solicited.

Respectfully submitted,

KLAUBER & JACKSON



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David A. Jackson  
Attorney for Applicants  
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PATENT  
600-1-266 N



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: MARY JEANNE KREEK ET AL.  
SERIAL NO.: 09/883,839 EXAMINER: UNASSIGNED  
FILED: June 18, 2001 ART UNIT: 1643  
FOR: ALLELES OF THE HUMAN MU OPIOID RECEPTOR,  
DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS  
OF TREATMENT BASED THEREON

Certificate of Mailing Under 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 on October 15, 2001.

David A. Jackson, Reg. No. 26.742  
(Name of Registered Rep.)

David A. Jackson, 10/15/01  
(Signature and Date)

PETITION FOR ONE-MONTH EXTENSION OF TIME

ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

Dear Sir:

Applicants hereby request that the period for responding to the Notice to File Missing Parts of Non-Provisional Application now set to expire on September 20, 2001, be extended by one (1) month, so as to expire on October 20, 2001.

As Applicants are associated with a small entity, a check in the amount of \$1,317.00 is enclosed to cover the fees involved in filing the One-Month Extension and Missing Parts of the Application. The Commissioner is further authorized to charge any deficiencies or to credit any overages to Deposit Account No. 11-1153.

PATENT  
600-1-266 N

Favorable action on this Request for Extension of Time is courteously solicited.

Respectfully submitted,

  
David A. Jackson  
Attorney for Applicant(s)  
Registration No. 26,742

KLAUBER & JACKSON  
411 Hackensack Avenue  
Hackensack, NJ 07601  
(201) 487-5800

Date:

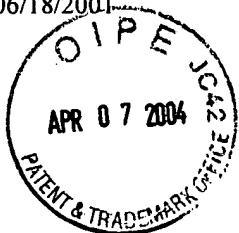


## UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS  
 UNITED STATES PATENT AND TRADEMARK OFFICE  
 WASHINGTON, D.C. 20231  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NUMBER	FLING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
09/883,839	06/18/2001	Mary Jeanne Kreek	600-1-266 N

23565  
 KLAUBER & JACKSON  
 411 HACKENSACK AVENUE  
 HACKENSACK, NJ 07601



CONFIRMATION NO. 9969

## FORMALITIES LETTER



\*OC000000006321355\*

Date Mailed: 07/20/2001

*File 9/20/01*  
*000 1/20/02*

## NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

*Filing Date Granted*

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.  
*Applicant must submit \$ 355 to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).*
- Total additional claim fee(s) for this application is \$1872.
  - \$657 for 73 total claims over 20.
  - \$1080 for 27 independent claims over 3 .
  - \$135 for multiple dependent claim surcharge.
- The oath or declaration is unsigned.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of \$65 for a small entity in compliance with 37 CFR 1.27, must be submitted with the missing items identified in this letter.
- **The balance due by applicant is \$ 2292.**

The application is informal since it does not comply with the regulations for the reason(s) indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- Substitute drawings in compliance with 37 CFR 1.84 because:
  - drawing sheets do not have the appropriate margin(s) (see 37 CFR 1.84(g)). Each sheet must include a top margin of at least 2.5 cm. (1 inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 1.5 cm. ( 5/8 inch), and a bottom margin of at least 1.0 cm. (3/8 inch);
- This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May

DOCKETED CPI